CLAIM AMENDMENTS DT04 Rec'd PCT/PTO 0 8 OCT 2004

- 1. (Original) A method for determining the concentration of a BNP precursor, or fragments thereof, in a sample obtained from a mammal, the method comprising treating the sample with an agent that cleaves the BNP precursor, and exposing the sample to an antibody that specifically binds to the cleaved product.
- 2. (Original) A method according to claim 1, wherein the cleaved product is any fragment of proBNP which can bind an antibody.
- 3. (Currently amended) A method according to claim 1 [[or 2]], wherein the fragment is at least 6 amino acids in length.
- 4. (Currently amended) A method according to <u>claim 1</u> any of the preceding elaims, wherein the antibody binds the N-terminus or the C-terminus of the cleaved product.
- 5. (Original) A method according to claim 4, wherein the antibody binds the N-terminus of proBNP1- 21.
- 6. (Currently amended) A method according to <u>claim 1</u> any of the preceding elaims, wherein the sample is selected from the group consisting of blood, serum, plasma, urine and a biopsy of the heart or other organs.
- 7. (Currently amended) A method according to <u>claim 1</u> any of the preceding claims, wherein the agent is any molecule that cleaves the BNP precursor to produce a fragment which can bind an antibody.
 - 8. (Original) A method according to claim 7, wherein the agent is an enzyme.
- 9. (Original) A method according to claim 8, wherein the enzyme is an serine protease selected from the group consisting of trypsin, furin, corin, yeast Kex2, prohormone convertase-1 and prohormone convertase-2.

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- 10. (Currently amended) A method <u>according to claim 1 wherein the for</u> determining the concentration of BNP precursors, or C terminally truncated fragments thereof, in a sample obtained from a mammal according to any of the preceding claims, the method comprising treating the sample with an agent that cleaves the precursor cleavers proteins at basic amino acids, and exposing the sample to an and the antibody [[that]] specifically binds an N-terminus of proBNP1-21.
- 11. (Currently amended) A method of predicting or diagnosing a cardiac disease, the method comprising performing the method of claim 1 according to any of the preceding claims, wherein elevated levels of antibody binding are indicative of cardiac dysfunction.
- 12. (Original) A method according to claim 11, wherein the cardiac dysfunction is selected from the group consisting of congestive heart failure, impaired function of the left ventricle, cardiac failure after myocardial infarction, arrhytmogenic right ventricular dysplasia, chronic respiratory disease due to tuberculosis, congenital heart disease, obstructive hypertrophic cardiomyopathy, predicting mortality in elderly and cardiac related acute dyspnea.
- 13. (Currently amended) A method of predicting or diagnosing a cardiac transplant rejection episode, the method comprising performing the method according to claim 1 [[1-10]], wherein an elevated level of antibody binding are indicative of a rejection episode.
- 14. (Currently amended) A method to [[ef]] distinguish between pulmonary and cardiovascular causes of dyspnea, the method comprising performing the method according to claim 1 any of claim 1-10, wherein elevated levels of antibody binding are indicative of cardiovascular causes of dyspnea.
- 15. (Currently amended) A method of predicting or diagnosing [[a]] <u>an</u> ischemic heart disease, the method comprising performing the method according to claim <u>1</u> [[1 10]], wherein elevated levels of antibody binding are indicative of a ischemic heart disease.

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- 16. (Currently amended) A method according to <u>claim 11</u>, any of claims 11–15 wherein an elevated level of antibody binding [[levels]] level is a levels above 15 pmol/L.
- 17. (Currently amended) A method for evaluating the effect of coronary angiography, the method comprising performing the method according to <u>claim 1</u> any of elaims 1-10, wherein the time of (blood) sampling is correlated in relation to invasive assessment.

Please add the following claims:

- 18. (New) A method according to claim 12, wherein an elevated level of antibody binding levels is a level above 15 pmol/L.
- 19. (New) A method according to claim 13, wherein an elevated level of antibody binding levels is a level above 15 pmol/L.
- 20. (New) A method according to claim 14, wherein an elevated level of antibody binding levels is a level above 15 pmol/L.
- 21. (New) A method according to claim 15, wherein an elevated level of antibody binding levels is a level above 15 pmol/L.

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